K101461

510(K) SUMMARY

JUN 24 2010

SUBMITTED BY: BECTON, DICKINSON AND COMPANY
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CONTACT NAME: Gregory P. Payne, RAC, Director Regulatory Affairs

DATE PREPARED: June 15, 2010

DEVICE TRADE NAME: BD Directigen™ EZ Flu A+B test

DEVICE COMMON NAME: Influenza virus serological reagents

DEVICE CLASSIFICATION: 21 CFR 866.3330

PREDICATE DEVICES : BD Directigen™ EZ Flu A+B test (K063689), (K042472)

INTENDED USE :

The BD Directigen™ EZ Flu A+B test is a rapid chromatographic immunoassay for the direct and qualitative detection of influenza A and B viral antigens from nasopharyngeal washes/aspirates, nasopharyngeal swabs and throat swabs of symptomatic patients. The Directigen™ EZ Flu A+B test is a differentiated test, such that influenza A viral antigens can be distinguished from influenza B viral antigens from a single processed sample using a single device. The test is to be used as an aid in the diagnosis of influenza A and B viral infections. All negative test results should be confirmed by cell culture because negative results do not preclude influenza virus infection and should not be used as the sole basis for treatment or other management decisions.

Performance characteristics for Influenza B using nasopharyngeal swabs (NPS) were established primarily with retrospective, frozen specimens. Users may wish to establish the sensitivity of this test for Influenza B using fresh nasopharyngeal swab specimens.

DEVICE DESCRIPTION :

The Directigen EZ Flu A+B test is a chromatographic assay to qualitatively detect influenza A and B viral antigens in samples processed from respiratory specimens. When specimens are processed and added to the test device, influenza A or B viral antigens bind to anti-influenza antibodies conjugated to visualizing particles in the corresponding A and B test strips. The antigen-conjugate complex migrates across the test strip to the reaction area and is captured by the line of antibody on the membrane. A positive result for influenza A is visualized as a reddish purple line at the Test "T" position and the Control "C" position in the Directigen EZ Flu A read window. A positive

result for influenza B is visualized as a reddish purple line at the Test "T" position and the Control "C" position in the Directigen EZ Flu B read window.

DEVICE COMPARISON:

The modified device differs from the currently marketed BD Directigen™ EZ Flu A+ B test in the following ways:

The labeling has been changed to reflect the addition of analytical sensitivity (LOD) data for A/California/4/2009 and A/California/7/2009 and the Strain Reactivity tables were updated accordingly.

In addition, instructions for the use of controls were modified to reflect the use of dry swab controls. The modification of the control material was under review at the same time as this submission and the modification has been cleared under K101529.

Modifications to the labeling are as follows:

Modification	Potential Impact of Change
1. Addition of data for analytical sensitivity and update to the strain reactivity tables for A/California/04/2009 and A/California/07/2009. A disclaimer was added: "although this test has been shown to detect the 2009 H1N1 virus cultured from a positive human respiratory specimen, the performance characteristics of this device with clinical specimens that are positive for the 2009 H1N1 influenza virus have not been established. The BD Directigen EZ Flu A+B test can distinguish between influenza A and B viruses, but it cannot differentiate influenza subtypes."	No impact to the assay kit because of addition of new data on LOD.
2. Labeling was changed to reflect a change of control from liquid to dry swab. Instructions for the use of controls were modified to reflect the use of dry swab controls. (K101529)	This modification was done under K101529. Verifcation and validation studies were conducted according to Design Control procedures to substantiate the modification of controls from liquid to dry swab. There was no impact on the assay.

SUMMARY OF THE STUDIES

This study was conducted by Professor JSM Peiris and Dr KH Chan at the Department of Microbiology, University of Hong Kong. A/California/4/2009 and A/California/7/2009 viruses were provided by the WHO Collaborating Centre for Surveillance, Epidemiology and Control of Influenza, US Centres for Disease Control and Prevention via the WHO Influenza Collaborating Centre, St Jude Children's Research Hospital, Memphis TN.

The identity of the cultured A/California/4/2009 and A/California/7/2009 viruses was confirmed using the CDC Swine Influenza Virus Real-time RTPCR Protocol for

Detection and Characterization of Swine Influenza and reagents supplied by the US CDC. Quantitative virus culture was done using MDCK cells grown on microtitre plates.

The Tissue Culture Infectious Dose ($TCID_{50}$) was determined according to the Reed and Muench Method.

The study was carried out using test-kits supplied by BD (Lot Number 9310845) according to the protocol supplied by the manufacturer. Undiluted virus culture of each virus was tested in triplicate using the BD Directigen EZ Flu A+B test. Then 10 fold dilutions of each virus were tested in singlicate. Half-log dilutions were prepared around the last dilution to be positive in the singlicate 10-fold dilution series and the test was repeated in triplicate. The test results were read by two independent operators.

The limit of detection of the BD Directigen EZ Flu A+B test on a pandemic H1N1 virus A/California/4/2009 infected MDCK cell culture with a $TCID_{50}$ titre of 6.23 Log 10 / mL was 3.5 Log10 and for A/California/7/2009 infected MDCK culture with a $TCID_{50}$ titre of 6.77 Log 10 / mL was 3.5 Log 10. Therefore, the limit of detection, expressed in $TCID_{50}$/mL, is $5.37X10^2$ for A/California/4/2009 and $1.86X10^3$ for A/California/7/2009.

SUBSTANTIAL EQUIVALENCE:

The modified device BD Directigen™ EZ Flu A+ B test is substantially equivalent to the current legally marketed device, BD Directigen™ EZ Flu A+B test. Additions made to the labeling to add additional strain testing did not change the intended use of the device or the fundamental scientific technology.

Risk analysis was not conducted to add this analytical sensitivity information to the product insert as no new issues of safety and effectiveness were identified for this addition to the product insert.

CONCLUSION

The results from this study indicate that the BD Directigen EZ Flu A+B test shows reactivity with cultured strains of A/California/4/09 and A/California/7/09 (2009 H1N1 influenza virus). The limit of detection (LOD) was demonstrated to be $5.37X10^2$ $TCID_{50}$/mL for A/California/4/09 strain and $1.86 X10^3$ $TCID_{50}$/mL for A/California/7/09 strain. Although this test has been shown to detect the 2009 H1N1 virus cultured from positive human respiratory specimens, the performance characteristics of this device with clinical specimens that are positive for the 2009 H1N1 influenza virus have not been established. The package insert for the device was revised to reflect the additional information.

The modified device BD Directigen™ EZ Flu A+ B test is substantially equivalent to the current legally marketed device, BD Directigen™ EZ Flu A+B test.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
10903 New Hampshire Avenue
Document Mail Center – WO66-0609
Silver Spring, MD 20993-0002

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Director, Regulatory Affairs and Quality Systems
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Re: k101461
Trade/Device Name: BD Directigen™ EZ Flu A+B Test
Regulation Number: 21 CFR 866.3330
Regulation Name: Influenza Virus Serological Reagents
Regulatory Class: Class I
Product Code: GNX
Dated: May 24, 2010
Received: May 26, 2010

Dear Mr. Payne:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

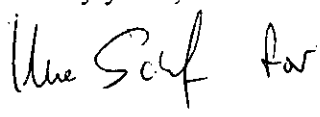
Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice

requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,



Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

INDICATION FOR USE

510(K) Number k101461

Device Name: BD Directigen™ EZ Flu A+B test

Indication for Use:

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Prescription Use__X__ 21 CFR 801 Subpart D)	And/or	Over the Counter Use____ (21 CFR 801Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Uwe Scherf

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

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